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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,787	01/31/2002	Nikos Pagratis	NEX87/PCT-US	6400

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EXAMINER	
FORMAN, BETTY J	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 05/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/030,787	PAGRATIS ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 2-7 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 2-7 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 31 January 2002 is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 1/02, 4/03.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. The preliminary amendment filed 30 April 2003 amended Claims 2-7 and canceled Claims 1 and 8-21.

Claims 2-7 are under prosecution.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

First Paragraph of 35 U.S.C. 112: Scope of Enablement

3. Claims 2-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making SEQ ID NO: 1-216, does not reasonably provide enablement for making and using the broadly claimed complexes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Breadth of the Claims

The claims are drawn to a complex comprising a TGFβ2 nucleic acid ligand and a non-immunogenic high molecular weight compound. The claims are written so broadly so as to encompass an enormous genus of nucleic acid sequences, a portion of which are ligands for

TGFβ2. The specification teaches SEQ ID NO: 1-216. However, the claims encompass, not only SEQ ID NO: 1-216, but also sequence comprising SEQ ID NO: 1-216 (e.g. a genome) and also includes sequences not described, defined or contemplated by the specification.

The claims also encompass an enormous genus of non-immunogenic high molecular weight compound including such compounds as a test tube or a microscope slide.

The specification teaches SEQ ID NO: 1-216 covalently linked to non-immunogenic compounds e.g. PEG, cholesterol, phospholipid, glycerol lipids (beginning at the bottom of page 12 through page 13) and the specification exemplifies a single ligand (NX22323) covalently linked to PEG (Example 5). However, the specification does not teach the broadly claimed complexes.

Nature of the Invention

The nature of the invention is such that nucleic acid ligands are selected using varying degrees of specificity between ligands and targets. However, the claims are drawn to complexes of any and all ligands of TGFβ2. The specification teaches that the selection and amplification "is continued until a selected goal is achieved" but the specification does not teach or describe the meets and bounds of those goals or obtained ligands so as to enable one of skill in the art to make and use the claimed invention.

"SELEX" methodology involves the combination of selection of nucleic acid ligands which interact with a target in a desirable manner, for example binding to a protein, with amplification of those selected nucleic acids, iterative cycling of the selection/amplification steps allows selection of one or a small number of nucleic acids which interact most strongly with the target from a pool which contains a very large number of nucleic acids. Cycling of the selection/amplification procedure is continued until a selected goal is achieved. In the present invention, the SELEX methodology is employed to obtain nucleic acid ligands to TGFβ2. (page 10, last paragraph).

Level of Predictability in the Art

The level of predictability in the art with respect to obtaining binding partners having functionality in a complex is very low because TGFβ2 belongs to a family of TGFβ proteins having 80% sequence homology, shared binding partners and shared signaling pathways. Furthermore, TGFβ2 has a structure "very similar to the structure of TGFβ1" (page 1, line 18-page 2, line 13). Given the similarities between the TGFβ family, the predictability with respect to TGFβ2-specific ligands would be very low.

Existence of Working Examples

The specification teaches SEQ ID NO: 1-216 covalently linked to non-immunogenic compounds e.g. PEG, cholesterol, phospholipid, glycerol lipids (beginning at the bottom of page 12 through page 13) and the specification exemplifies a single ligand (NX22323) covalently linked to PEG (Example 5). However, the specification does not teach working examples of the broadly claimed complexes. Therefore, the specification does not provide working examples of the claimed invention that would enable one of ordinary skill in the art to make and use the invention as claimed.

Quantity of Experimentation Required

The claims are drawn to a complex comprising a TGFβ2 nucleic acid ligand and a non-immunogenic high molecular weight compound. In view of the breadth of the claims being drawn to an enormous genus of nucleic acid sequences, an enormous genus of high molecular weight compounds and, hence, an enormous genus of complexes; in view of the nature of the invention wherein ligands have a wide variety of target specificity; in view of the of unpredictability in the art with regard to target-binding due to the similarity within the TGFβ family; and in view of the lack of working examples of the broadly claimed invention, it would require undue experimentation for one skilled in the art to make and use the invention as claimed.

First paragraph of 35 U.S.C. 112: Written Description

4. Claims 2-7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a complex of TGFb2 nucleic acid ligand and non-immunogenic, high molecular weight compound. The specification does not provide and adequate written description of the claimed invention.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention is complete as evidenced by drawings or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention.

Reduction to practice

The claims are drawn to a complex of TGFb2 nucleic acid ligand and non-immunogenic, high molecular weight compound. The specification does not describe an actual reduction to practice of the broadly claimed invention. The specification teaches SEQ ID NO: 1-216 covalently linked to non-immunogenic compounds e.g. PEG, cholesterol, phospholipid, glycerol lipids (beginning at the bottom of page 12 through page 13) and the specification exemplifies a single ligand (NX22323) covalently linked to PEG (Example 5). However, the claims are drawn to an enormous genus of complexes which are not exemplified.

Completed by drawings

The specification does not teach that the invention is complete as evidenced by drawings. The drawings of the specification illustrate some of the nucleic acid ligands taught in the specification e.g. SEQ ID NO: 72, 86, 87, 93, 115, 131, 144, 216: Fig. 7-10) and the tables list SEQ ID NO: 1-216. However, neither the drawings or tables illustrate the broadly claimed nucleic acid ligand complexes.

Description of identifying characteristics

The specification has not been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention. The specification teaches methods for isolating target-specific nucleic acid ligands (Examples 2-3) and the specification teaches selection of target-specific ligands until ligands of relatively high affinity for the target are obtained (page 11).

However the specification does not a describe identifying characteristics of the claimed complexes which show that applicant was in possession of the claimed complexes. Therefore, the specification does not provide a written description of the claimed invention in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The courts have stated that the specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonable conclude the inventor had possession of the claimed invention see *In re Vas-Cath*, Inc. 935F2d. 1555, 1563, 19 USPQ2d 1111,1116

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 2-7 are rejected under 35 U.S.C. 102(e) as being anticipated by Gold et al (U.S. Patent No. 6,124,449, filed 23 March 1998)

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The claims are drawn to a complex comprising nucleic acid ligands to TGFβ2 and a non-immunogenic high molecular weight compound. The specification describes complexes comprising nucleic acid ligands (SEQ ID NO: 1-216) and PEG.

Regarding Claim 2-7, Gold discloses nucleic acid ligands of TGFβ2 and a non-immunogenic high molecular weight compound e.g. PEG (Column 10, lines 10-44).

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 2-7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2-14 of U.S. Patent No. 6,713,616. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a complex comprising a nucleic acid ligand of TGFβ2 and a non-immunogenic high molecular weight compound. The claims only differ in that the patent claims describe the ligands as SEQ ID NO: 194-215. Though the conflicting claims are not identical, they are not patentably distinct from each other because the ligands to TGFβ2 to which both sets of claims are drawn have the same nucleotide sequences and the same complexing PEG. The claims, if allowed, would improperly extend the "right to exclude" already granted in the patent. The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter.

9. Claims 2-7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim1-5 of U.S. Patent No. 6,346,611. Although the

conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a complex comprising a nucleic acid ligand of TGFβ2 and a non-immunogenic high molecular weight compound. The claims only differ in that the patent claims describe the ligands as SEQ ID NO: 21-121 and 128-193. Though the conflicting claims are not identical, they are not patentably distinct from each other because the ligands to TGFβ2 to which both sets of claims are drawn have the same nucleotide sequences and the same complexing PEG. The claims, if allowed, would improperly extend the "right to exclude" already granted in the patent. The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter.

10. Claims 2-7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,124,449. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a nucleic acid ligand of TGFβ2. The claims only differ in that the patent claims describe the ligands as SEQ ID NO: 6-143) and the instant claims are further drawn to the ligands complexed with non-immunogenic high molecular weight compound. Though the conflicting claims are not identical, they are not patentably distinct from each other because the ligands to TGFβ2 to which both sets of claims are drawn have the same nucleotide sequences and because the patent teaches the preferred form of the ligands is complexed to a non-immunogenic high molecular weight compound (Column 10, lines 25-44). Hence, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the patent ligands by complexing the ligands with a non-

immunogenic high molecular weight compound based on the patents preferred form for the patented ligands (Column 10, lines 25-44).

11. Claims 2-7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 5,731,424 in view of Gold et al (U.S. Patent No. 6,124,449). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a nucleic acid ligand of TGFβ. The claims only differ in that the instant claims are further drawn to the ligands complexed with non-immunogenic high molecular weight compound. Though the conflicting claims are not identical, they are not patentably distinct from each other because the ligands to TGFβ to which both sets of claims are drawn are the same and because the Gold et al teaches the preferred form of nucleic acids ligands is complexed to a non-immunogenic high molecular weight compound (Column 10, lines 25-44). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the patent ligands by complexing with a non-immunogenic high molecular weight compound based on Gold's preferred form nucleic acid ligands (Column 10, lines 25-44).

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
May 24, 2004